REMARKS

Claims 1-25 are pending in this application.

All the pending claims stand rejected in the Office Action as being unpatentable under 35 USC §103(a) over Decker et al. (Clin. Cancer Res. 5:1169-1192, 1999) in view of Corominas et al. (J. Bio. Chem. 260(30):16269-16273, 1985) and Armstrong et al. (Anal. Biochem. 292:26-33, 2001). All the pending claims are also rejected under 35 U.S.C. 103(a) as being unpatentable over Trevigen (Universal Colorimetric PARP Assay kit with histones and coating buffer, 2000) in view of Armstrong et al. (supra), Sundberg (Current Opinion in Biotechnology, 2000, 11 :47-53) and Human Molecular Genetics (Fluorescence labeling and detection system, 1 999; http://lwww.ncbi.nlm.nih.gov/books/bv.fegi?rid=hmg.table.479) Applicants respectfully traverse these rejections on the grounds that the Office Action fails to establish a *prima facie* case of obviousness for any of the pending claims.

Rejections under 35 U.S.C. 103(a)

I. As being unpatentable over Decker et al. in view of Corominas et al. and Armstrong et al.

The Examiner finds Applicants' response on April 13, 2006 "not persuasive because the method of Decker et al. does not take longer incubation time as Applicant pointed out. In fact, Fig. 1 of Decker et al. shows the incubation time for PARP, NAD substrate and an inhibitor takes only 1 hr at 4°C (see also p 1170; Materials and Methods). Applicant's argument that the method of Decker et al. takes overnight or at least more than 7 hours is the total assay duration rather than the incubation duration."

The Examiner repeats the rejections:

Decker discloses a PARP inhibition assay which differs from that recited in the claims in that Decker does not use fluorescently labeled NAD in the quantification of enzyme activity. See, e.g., Fig 1, on page 1170. However, Corominas et al. clearly discloses that labeled NAD can be used in the quantification of PARP activity. See, e.g., page 16270, left column. Moreover, Armstrong discloses the use of fluorescently labeled NAD in an assay of ADP-ribosylating enzyme, an assay which detects similar activity to that of both Decker and Corominas. See, e.g., page 28. Thus, the artisan of ordinary skill would have considered it obvious to have used fluorescently labeled NAD in the quantification of enzyme activity in Decker's assay, motivation for such practice being derived from Corominas' disclosure of the suitability of labeled NAD as detection moiety in PARP assays, and from Armstrong's disclosure of the

suitability of fluorescently labeled NAD as a detection moiety in a similar assay of ADP-ribosylating enzyme.

In the previous response to Office action, Applicants have pointed out that the applied references fail to teach or suggest all the claim limitations and there is no suggestion or motivation to modify or combine reference teachings to produce claimed invention. A *prima facie* case of obviousness fails for at least following reasons. First, Decker et al. teaches a multiple step method with requires repetitive washing steps and long duration time (total assay duration time over 7 hours or overnight) : i) immobilize human rPARP onto microtiter place; ii) wash 3 times; iii) add β-NAD^+ and buffer and incubate at 4°C for 1 hour; iv) wash 3 times ; v) detect by adding the antibody to mix; vi) incubate more than 1 hour and wash 3 times; vii) add IgG3 for 30 min; viii) washing again; ix) visualize the plates; x) stop the reaction and measure the absorbance (see the reference of Decker et al. "MATERIALS AND METHODS" p1171). The claimed invention features a fluorescent assay which is a simple screening assay with remarkable short reaction time (10 minutes or above) (see Application, p3, line 18-20). The claimed invention is a simple 3 step assay: i) mix all reagents and incubate for 10 min; ii) measure the mixture; iii) compare the result. The method of claimed invention eliminates repetitive washing steps and requires much shorter duration time, therefore it is obviously advantageous to the method of Decker et al.

According to MPEP 2141, when applying 35 U.S.C. §103, the following tenets of patent law must be adhered to:

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) Reasonable expectation of success is the standard with which obviousness is determined.

Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986)

Applicants clearly state the claimed invention is a simple fluorescent screening assay with remarkably short duration time. When a reference is considered for 35 U.S.C. 103

rejection, "*The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination*". Apparently, Decker et al. neither teach a simple screening assay nor suggest the desirability of this kind.

> The Examiner states that "the teaching of Corominas et al. in support of the method of Decker et al. is a labeled NAD+. Corominas et al. disclose NAD+ can be used as a labeled NAD+. The use of labeled NAD+ is more efficient than the use of a non-labeled NAD+ in PARP assay because it can be directly detected without employing another step using an anti-poly(ADP-ribose) and a secondary antibody against the anti-poly(ADP-ribose). Therefore, there is a motivation for a person of ordinary skill in the art to use a labeled NAD+ in the method of Decker et al."

Accordingly, the teaching of Corominas et al. in support of the method of Decker et al. is a labeled NAD+ in the method of Decker et al. does not remedy the deficiencies of Decker et al. of *multiple step method* with *repetitive washing steps* and *long duration time*.

> The Examiner agrees with Applicant that the mechanism and assay system utilized by Armstrong et al. are different from the claimed invention. But the Examiner further states that it is not the whole teaching of Armstrong et al. used in the combination with the method of Decker et al. in view of Corominas et al. and the subject matter would have been adopted from this reference by Decker et al. in view of Corominas et al. is a fluorescence-labeled NAD+.

Applicants respectively point out that the whole teaching of Armstrong et al. used in the combination with the method of Decker et al. in view of Corominas et al. may teach a fluorescence-labeled NAD+ essay, but it does not teach or suggest a simple screening assay with remarkably short duration time. Therefore, either each reference alone or the combination of these references does not teach or suggest the claimed invention, and does not remedy the deficiencies of Decker et al. of multiple step method with long duration time.

As discussed in *Response to the Examiner's response to Arguments (on Applicants' response on April 13, 2006)*, considering the claimed invention as a whole, the combined references do not teach or suggest the claimed invention which features a simple fluorescent screening assay with remarkable short duration time. Decker et al. teaches a ***multiple*** step method which requires repetitive washing steps and long duration time, and Corominas et al. and Armstrong et al. do not remedy the deficiencies of Decker et al. of the multiple step method with long duration time.

II. As being unpatentable over Trevigen (Universal Colorimetric PARP Assay kit)

The Examiner states:

> The Trevigen reference teaches a method of determining inhibitors on the activity of PARP comprising steps of incubation of PARP enzyme, an inhibitor, a substrate (biotinylated NAD+, DNA, histone), detection of enzymatic activity, and comparison of the measurement (see pages 1-4). The Trevigen article does not teach the use of fluorescently labeled NAD+ in an assay. Armstrong et al. teach the use of fluorescently labeled NAD in an assay of ADP ribosylating enzyme. Sundberg teaches fluorescence-based biochemical assays. It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute biotinylated NAD+ of Trevigen with fluorescently labeled NAD+ of Armstrong et al. in the method of Trevigen Instruction.

Applicants respectively dispute with this assertion. The Trevigen reference teaches a method based on time-consuming and cumbersome ELISA-Like principle. The referenced method constitutes 10 steps including i) coating plate; ii) washing 4 times; iii) blocking plates; iv) washing again; v) enzyme reaction; vi) washing 4 times; vii) binding reaction; viii) washing; ix) detecting; x) reading. The method of Trevigen, similar to the method of Decker et al. with repetitive washing steps and long duration time, teaches away from the claimed invention. To establish *prima facie* obviousness of a claimed invention, all claim limitation must be taught or suggested. Apparently, The Trevigen reference does not teach a simple fluorescent screening assay with remarkably short duration time.

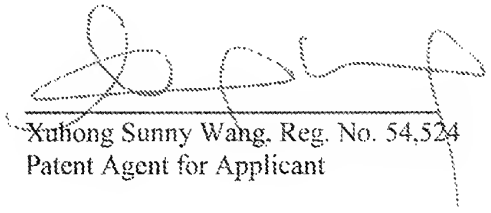
Sundberg et al. discusses the trend towards assay for high-throughput and ultra-high-throughput screening and does not remedy the deficiencies of Trevigen reference of the multiple step method with requires repetitive washing steps and long duration time. The combined references do not teach or suggest the claimed invention which features a simple fluorescent screening assay with remarkably short duration time.

In summary, Applicants respectively traverse the rejections. Applicants urge the Examiner to consider the claimed invention as a whole which is not only a fluorescent assay with NAD+ labeling but also a simple screening assay with remarkably short duration time. The claimed invention is advantageous over existing assays which are either published or commercially available.

Thus, it is believed that rejection has been overcome. Withdrawal of this rejection is respectively requested. Applicants respectfully submit that the application is now in condition

for allowance and request prompt notice thereof. Should the Examiner believe that an interview would advance the prosecution of this application, the Applicants invite him to contact the undersigned at 908.231.3648.

Respectfully submitted,



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